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Positivity

Positive semigroups and perturbations of boundary conditions

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Abstract
We present a generation theorem for positive semigroups on an L^1 space. It provides sufficient conditions for the existence of positive and integrable solutions of initial-boundary value problems. An application to a two-phase cell cycle model is given.

Keywords Positive semigroup · Perturbation of boundary conditions · Steady state · Cell cycle models

Mathematics Subject Classification 47B65 · 47H07 · 47D06 · 92C40

1 Introduction

We study well-posedness of linear evolution equations on L^1 of the form

$$u'(t) = Au(t), \quad \Psi_0 u(t) = \Psi u(t), \quad t > 0, \quad u(0) = f, \tag{1}$$

where Ψ_0, Ψ are positive and possibly unbounded linear operators on L^1, the linear operator A is such that Eq. (1) with $\Psi = 0$ generates a *positive semigroup* on L^1, i.e., a C_0-semigroup of positive operators on L^1. We present sufficient conditions for the operators A, Ψ_0, and Ψ under which there is a unique positive semigroup on L^1 providing solutions of the initial-boundary value problem (1). For a general theory of

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positive semigroups and their applications we refer the reader to [4,7,11,14,34]. An overview of different approaches used in studying initial-boundary value problems is presented in [13].

Our result is an extension of Greiner's [19] by considering unbounded Ψ and positive semigroups. Unbounded perturbations of the boundary conditions of a generator were studied recently in [1,2] by using extrapolated spaces and various admissibility conditions. In the proof of our perturbation theorem we apply a result about positive perturbations of resolvent positive operators [3] with non-dense domain in AL-spaces in the form given in [37, Theorem 1.4]. It is an extension of the well known perturbation result due to Desch [15] and by Voigt [41]. For positive perturbations of positive semigroups in the case when the space is not an AL-space we refer to [5,10]. We also present a result about stationary solutions of (1). We illustrate our general results with an age-size-dependent cell cycle model generalizing the discrete time model of [22,25,38]. This model can be described as a piecewise deterministic Markov process (see Sect. 5 and [34]). Our approach can also be used in transport equations [8,23].

2 General results

Let $(E, \mathcal{E}, m)$ and $(E_\partial, \mathcal{E}_\partial, m_\partial)$ be two σ-finite measure spaces. Denote by $L^1 = L^1(E, \mathcal{E}, m)$ and $L^1_\partial = L^1(E_\partial, \mathcal{E}_\partial, m_\partial)$ the corresponding spaces of integrable functions. Let $\mathcal{D}$ be a linear subspace of L^1. We assume that $A : \mathcal{D} \to L^1$ and $\Psi_0, \Psi : \mathcal{D} \to L^1_\partial$ are linear operators satisfying the following conditions:

(i) for each $\lambda > 0$, the operator $\Psi_0 : \mathcal{D} \to L^1_\partial$ restricted to the nullspace $\mathcal{N}(\lambda I - A) = \{f \in \mathcal{D} : \lambda f - Af = 0\}$ of the operator $(\lambda I - A, \mathcal{D})$ has a positive right inverse, i.e., there exists a positive operator $\Psi(\lambda) : L^1_\partial \to \mathcal{N}(\lambda I - A)$ such that $\Psi_0 \Psi(\lambda) f_\partial = f_\partial$ for $f_\partial \in L^1_\partial$;
(ii) the operator $\Psi : \mathcal{D} \to L^1_\partial$ is positive and there exists $\omega \in \mathbb{R}$ such that the operator $I_\partial - \Psi\Psi(\lambda) : L^1_\partial \to L^1_\partial$ is invertible with positive inverse for all $\lambda > \omega$, where I_∂ is the identity operator on L^1_∂;
(iii) the operator $A_0 \subseteq A$ with $\mathcal{D}(A_0) = \{f \in \mathcal{D} : \Psi_0 f = 0\}$ is the generator of a positive semigroup on L^1;
(iv) for each nonnegative $f \in \mathcal{D}$

$$\int_E Af(x)\, m(dx) - \int_{E_\partial} \Psi_0 f(x)\, m_\partial(dx) \le 0. \tag{2}$$

Theorem 1 *Assume conditions* (i)–(iv). *Then the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ defined by*

$$A_\Psi f = Af, \quad f \in \mathcal{D}(A_\Psi) = \{f \in \mathcal{D} : \Psi_0(f) = \Psi(f)\}, \tag{3}$$

is the generator of a positive semigroup on L^1. Moreover, the resolvent operator of A_Ψ at $\lambda > \omega$ is given by

$$R(\lambda, A_\Psi) f = (I + \Psi(\lambda)(I_\partial - \Psi\Psi(\lambda))^{-1}\Psi) R(\lambda, A_0) f, \quad f \in L^1. \tag{4}$$

Proof The space $\mathcal{X} = L^1 \times L^1_\partial$ is an AL-space with norm

$$\|(f, f_\partial)\| = \int_E |f(x)|\, m(dx) + \int_{E_\partial} |f_\partial(x)|\, m_\partial(dx), \quad (f, f_\partial) \in L^1 \times L^1_\partial.$$

We define operators $\mathcal{A}, \mathcal{B} \colon \mathcal{D}(\mathcal{A}) \to L^1 \times L^1_\partial$ with $\mathcal{D}(\mathcal{A}) = \mathcal{D} \times \{0\}$ by (see e.g. [34])

$$\mathcal{A}(f, 0) = (Af, -\Psi_0 f) \quad \text{and} \quad \mathcal{B}(f, 0) = (0, \Psi f) \quad \text{for } f \in \mathcal{D}.$$

We have $\mathcal{D}(A_0) \times \{0\} \subset \mathcal{D}(\mathcal{A}) \subset L^1 \times \{0\}$ and $\mathcal{D}(A_0)$ is dense in L^1. Hence, $\overline{\mathcal{D}(\mathcal{A})} = L^1 \times \{0\}$. For every $\lambda > 0$ the resolvent of the operator $\mathcal{A}$ at $\lambda > 0$ is given by

$$R(\lambda, \mathcal{A})(f, f_\partial) = (R(\lambda, A_0) f + \Psi(\lambda) f_\partial, 0), \quad (f, f_\partial) \in L^1 \times L^1_\partial. \tag{5}$$

Thus $(\mathcal{A}, \mathcal{D}(\mathcal{A}))$ is resolvent positive, i.e., its resolvent operator $R(\lambda, \mathcal{A})$ is positive for all sufficiently large $\lambda > 0$. We now show that$\|\lambda R(\lambda, \mathcal{A})\| \le 1$ for all $\lambda > 0$. Since the operator $\lambda R(\lambda, \mathcal{A})$ is positive, it is enough to show that

$$\|\lambda R(\lambda, \mathcal{A})(f, f_\partial)\| \le \|(f, f_\partial)\| \quad \text{for nonnegative } (f, f_\partial) \in L^1 \times L^1_\partial. \tag{6}$$

The operator $R(\lambda, A_0)$ is positive, $R(\lambda, A_0) f \in \mathcal{D}(A_0) \subseteq \mathcal{D}$ and $\Psi_0 R(\lambda, A_0) f = 0$ for $f \in L^1$. From this and (2) we see that

$$\int_E AR(\lambda, A_0) f(x)\, m(dx) \le \int_{E_\partial} \Psi_0 R(\lambda, A_0) f(x)\, m_\partial(dx) = 0$$

for all nonnegative $f \in L^1$. We have $AR(\lambda, A_0) f = \lambda R(\lambda, A_0) f - f$ for all $f \in L^1$, by (iii). Thus, we get

$$\begin{aligned}\int_E \lambda R(\lambda, A_0) f(x)\, m(dx) &= \int_E AR(\lambda, A_0) f(x)\, m(dx) + \int_E f(x)\, m(dx)\\ &\le \int_E f(x)\, m(dx), \quad f \in L^1,\ f \ge 0.\end{aligned}$$

By assumption (i), $A\Psi(\lambda) f_\partial = \lambda \Psi(\lambda) f_\partial$ and $\Psi_0 \Psi(\lambda) f_\partial = f_\partial$ for $f_\partial \in L^1_\partial$. This together with condition (2) implies that

$$\begin{aligned}\int_{E_\partial} \lambda \Psi(\lambda) f_\partial(x)\, m_\partial(dx) &= \int_E A\Psi(\lambda) f_\partial(x)\, m(dx) \le \int_{E_\partial} \Psi_0 \Psi(\lambda) f_\partial(x)\, m_\partial(dx)\\ &= \int_{E_\partial} f_\partial(x)\, m_\partial(dx)\end{aligned}$$

for all nonnegative $f_\partial \in L^1_\partial$, completing the proof of (6).

Let $\mathcal{I}$ be the identity operator on $\mathcal{X} = L^1 \times L^1_\partial$. We have $\mathcal{B}R(\lambda, \mathcal{A})(f, f_\partial) = (0, \Psi R(\lambda, A_0) f + \Psi \Psi(\lambda) f_\partial)$ for any (f, f_∂). Thus, $\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A})$ is invertible if and only if $I_\partial - \Psi\Psi(\lambda)$ is invertible. In that case

$$(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}(f, f_\partial) = (f, (I_\partial - \Psi\Psi(\lambda))^{-1}(\Psi R(\lambda, A_0) f + f_\partial)).$$

Combining this with (ii) we conclude that $\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A})$ is invertible with positive inverse $(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}$ for all $\lambda > \omega$. Hence, the spectral radius of the positive operator $\mathcal{B}R(\lambda, \mathcal{A})$ is strictly smaller than 1 for some $\lambda > \omega$. It follows from [37, Theorem 1.4] that the part of $(\mathcal{A} + \mathcal{B}, \mathcal{D}(\mathcal{A}))$ in $\mathcal{X}_0 = \overline{\mathcal{D}(\mathcal{A})}$ denoted by $((\mathcal{A} + \mathcal{B})_|, \mathcal{D}((\mathcal{A} + \mathcal{B})_|))$ generates a positive semigroup on $\mathcal{X}_0$. We have $\mathcal{D}((\mathcal{A} + \mathcal{B})_|) = \mathcal{D}(A_\Psi) \times \{0\}$ and $(\mathcal{A} + \mathcal{B})_|(f, 0) = (A_\Psi f, 0)$, $f \in \mathcal{D}(A_\Psi)$. Consequently, the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is densely defined and generates a positive semigroup on L^1. Finally, the operator $(\mathcal{A} + \mathcal{B}, \mathcal{D}(\mathcal{A}))$ is resolvent positive with resolvent given by $R(\lambda, \mathcal{A} + \mathcal{B}) = R(\lambda, \mathcal{A})(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}$ for $\lambda > \omega$. Hence, the formula for $R(\lambda, A_\Psi)$ is also valid. □

Remark 1 Condition (iv) ensures that the operator $(A_0, \mathcal{D}(A_0))$ satisfies

$$\int_E A_0 f(x) m(dx) \leq 0 \tag{7}$$

for all nonnegative $f \in \mathcal{D}(A_0)$. If, additionally,

(v) $(A_0, \mathcal{D}(A_0))$ is densely defined and resolvent positive,

then $(A_0, \mathcal{D}(A_0))$ is the generator of a *substochastic semigroup* on L^1, i.e., a positive semigroup of contractions on L^1. This is a consequence of the Hille–Yosida theorem, see e.g. [34, Theorem 4.4]. Thus it is enough to assume condition (v) instead of (iii). Observe also that (iii) and (iv) imply that $(0, \infty) \subseteq \rho(A_0)$.

Remark 2 Note that if $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup and

$$\int_E A_\Psi f(x) m(dx) = 0 \quad \text{for all nonnegative } f \in \mathcal{D}(A_\Psi), \tag{8}$$

then $(A_\Psi, \mathcal{D}(A_\Psi))$ generates a *stochastic semigroup*, i.e., a positive semigroup of operators preserving the L^1 norm of nonnegative elements (see e.g. [7, Section 6.2] and [34, Corollary 4.1]).

Remark 3 If we assume that

(a) $(A, \mathcal{D})$ is closed,
(b) Ψ_0 is onto and continuous with respect to the graph norm $\|f\|_A = \|f\| + \|Af\|$,

then $\Psi(\lambda)$ exists for each $\lambda > 0$ and is bounded, by [19, Lemma 1.2]. If Ψ_0 is positive, then $\Psi(\lambda)$ is positive. Thus condition (i) can be replaced by conditions (a) and (b).

Remark 4 Greiner [19, Theorem 2.1] establishes that $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a C_0-semigroup for any bounded Ψ provided that conditions (a) and (b) hold true, $(A_0, \mathcal{D}(A_0))$ is the generator of a C_0-semigroup, and that there exist constants $\gamma > 0$ and λ_0 such that

$$\|\Psi_0 f\| \geq \lambda\gamma\|f\|, \quad f \in \mathcal{N}(\lambda I - A), \lambda > \lambda_0. \tag{9}$$

This is condition (2.1) of Greiner [19, Theorem 2.1]. Some extensions of this result are provided in [20,29] for unbounded Ψ, as well as in [1,2].

Remark 5 Recall that a positive operator on an AL-space defined everywhere is automatically bounded. Thus our assumption (i) implies that $\Psi(\lambda)$ is bounded for each $\lambda > 0$. Moreover, its norm is determined through its values on the positive cone. From assumptions (i) and (iv) it follows that $\lambda\|\Psi(\lambda)\| \leq 1$ for each $\lambda > 0$, as was shown in the proof of Theorem 1. Thus, for $f = \Psi(\lambda) f_\partial$, we get (9) with $\gamma = 1$. Now suppose, as in [19], that Ψ is bounded. Then $\|\Psi\Psi(\lambda)\| \leq \|\Psi\|/\lambda$ for all $\lambda > 0$. Hence, the operator $I_\partial - \Psi\Psi(\lambda)$ is invertible for $\lambda > \|\Psi\|$. Since $I - \Psi(\lambda)\Psi$ is also invertible, we have $(I - \Psi(\lambda)\Psi)^{-1} = I + \Psi(\lambda)(I_\partial - \Psi\Psi(\lambda))^{-1}\Psi$ and, by (4),

$$R(\lambda, A_\Psi) = (I - \Psi(\lambda)\Psi)^{-1} R(\lambda, A_0).$$

Consequently, if Ψ is bounded and positive, then we get the same result as in [19].

We now look at a simple example where Theorem 1 can be easily applied and it should be compared with [1, Corollary 25].

Example 1 Consider the space $L^1 = L^1[0, 1]$ and the first derivative operator $A = \frac{d}{dx}$ with domain $\mathcal{D} = W^{1,1}[0, 1]$. Let E_∂ be the one point set $\{1\}$ and m_∂ be the point measure δ_1 at 1, so that the boundary space is $L^1_\partial = \{f_\partial : \{1\} \to \mathbb{R} : f_\partial(1) \in \mathbb{R}\}$ and can be identified with $\mathbb{R}$, by writing $f_\partial = f_\partial(1)$. Let the boundary operators Ψ_0 and Ψ be defined by

$$\Psi_0 f = f(1) \quad \text{and} \quad \Psi f = \int_{[0,1]} f(x)\mu(dx), \quad f \in W^{1,1}[0, 1],$$

where μ is a finite Borel measure. Note that for each $\lambda > 0$ and $f \in \mathcal{N}(\lambda I - A)$ we have $f' = \lambda f$. Thus f' is a continuous function. Consequently, for each $f_\partial \in L^1_\partial$ and $\lambda > 0$, the solution $f = \Psi(\lambda) f_\partial$ of equation $f' = \lambda f$ satisfying $\Psi_0(\lambda) f = f_\partial$ is of the form

$$\Psi(\lambda) f_\partial(x) = e^{\lambda(x-1)} f_\partial, \quad x \in [0, 1].$$

Hence condition (i) holds true. We have

$$\int_{[0,1]} Af(x)dx = f(1) - f(0), \quad f \in W^{1,1}[0, 1],$$

and the restriction A_0 of the operator A to

$$\mathcal{D}(A_0) = \{f \in W^{1,1}[0,1] : f(1) = 0\}$$

is the generator of a positive semigroup. Thus conditions (iii) and (iv) hold true. If there exists $\lambda > 0$ such that

$$\int_{[0,1]} e^{\lambda(x-1)} \mu(dx) < 1, \tag{10}$$

then condition (ii) holds true and the operator $A_\Psi \subseteq \frac{d}{dx}$ with domain

$$\mathcal{D}(A_\Psi) = \{f \in W^{1,1}[0,1] : f(1) = \int_{[0,1]} f(x)\mu(dx)\}$$

is the generator of a positive semigroup, by Theorem 1. Now suppose that μ is a probability measure, so that $\mu([0,1]) = 1$. Then

$$\int_{[0,1]} e^{\lambda(x-1)} \mu(dx) \le 1$$

for all $\lambda > 0$. Thus if (10) does not hold for any $\lambda > 0$ then $e^{\lambda(x-1)} = 1$ for all $\lambda > 0$ and μ-almost every $x \in [0,1]$ implying that $\mu\{x \in [0,1] : x = 1\} = 1$. Consequently, if μ is a probability measure such that $\mu \neq \delta_1$ then $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup.

It should be noted that in [34, Theorem 4.6] the assumption that the domain $\mathcal{D}(A_\Psi)$ of the operator A_Ψ is dense is missing. Making use of Theorem 1, we get the following result.

Theorem 2 *Assume conditions* (i)–(iv). *If B is a bounded positive operator such that*

$$\int_E (A_\Psi f(x) + Bf(x)) m(dx) \le 0 \quad \textit{for all nonnegative } f \in \mathcal{D}(A_\Psi),$$

then $(A_\Psi + B, \mathcal{D}(A_\Psi))$ is the generator of a substochastic semigroup.

We conclude this section with a result concerning the existence of steady states of the positive semigroup from Theorem 1. Note that given any $\lambda, \mu \in \rho(A_0)$ we have $\Psi(\lambda) = \Psi(\mu) + (\mu - \lambda)R(\lambda, A_0)\Psi(\mu)$, see [19, Lemma 1.3]. Thus $\Psi(\lambda) \ge \Psi(\mu)$ for $\lambda \le \mu$. Consequently, for each nonnegative $f_\partial \in L^1_\partial$ the pointwise limit

$$\Psi(0) f_\partial = \lim_{\lambda \to 0^+} \Psi(\lambda) f_\partial \tag{11}$$

exists and $\Psi(0) f_\partial$ is nonnegative.

Theorem 3 *Assume conditions* (i)–(iv). *Let* $\Psi(0)$ *be as in* (11). *If a nonnegative* $f_\partial \in L^1_\partial$ *satisfies* $\Psi(0)f_\partial \in L^1$ *and* $f_\partial = \Psi\Psi(0)f_\partial$, *then* $\Psi(0)f_\partial \in \mathcal{D}(A_\Psi)$ *and* $A_\Psi\Psi(0)f_\partial = 0$. *Conversely, if* $A_\Psi f = 0$ *for a nonnegative* $f \in \mathcal{D}(A_\Psi)$ *then* $f_\partial = \Psi f$ *satisfies* $\Psi\Psi(\lambda)f_\partial \le f_\partial$ *for all* $\lambda > \max\{0,\omega\}$, *where* ω *is as in* (ii).

Proof It follows from condition (i) that $\Psi(\lambda)f_\partial \in \mathcal{D}$, $\Psi_0\Psi(\lambda)f_\partial = f_\partial$, and $A\Psi(\lambda)f_\partial = \lambda f_\partial$ for all $\lambda > 0$. We have $\Psi(\lambda)f_\partial \to \Psi(0)f_\partial$ in L^1, as $\lambda \to 0$. Thus $A\Psi(\lambda)f_\partial \to 0$ in L^1, as $\lambda \to 0$. Recall from the proof of Theorem 1 that the operator $(\mathcal{A}+\mathcal{B})(f,0) = (Af, \Psi f - \Psi_0 f)$, $f \in \mathcal{D}$, is a closed operator in the space $L^1 \times L^1_\partial$. The operators Ψ and Ψ_0 are positive and we have $\Psi\Psi(\lambda)f_\partial \to \Psi\Psi(0)f_\partial = f_\partial = \Psi_0\Psi(0)f_\partial$. Thus, $(\mathcal{A}+\mathcal{B})(\Psi(\lambda)f_\partial, 0) \to (0,0)$ as $\lambda \to 0$. This implies that $\Psi(0)f_\partial \in \mathcal{D}(A_\Psi)$ and $A_\Psi\Psi(0)f_\partial = 0$.

For the converse, suppose that $f \in \mathcal{D}(A_\Psi)$ and $A_\Psi f = 0$. We have $R(\lambda, A_\Psi)(\lambda f - A_\Psi f) = 0$. Thus $\lambda R(\lambda, A_\Psi)f = f$ and $\Psi f = \Psi R(\lambda, A_\Psi)(\lambda f) = \Psi R(\lambda, A_0)(\lambda f) + \Psi\Psi(\lambda)(I_\partial - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f)$, by (4). Since

$$\Psi R(\lambda, A_0)(\lambda f) = (I_\partial - \Psi\Psi(\lambda))(I_\partial - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f),$$

we conclude that $\Psi f = (I_\partial - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f)$. This implies that $(I_\partial - \Psi\Psi(\lambda))\Psi f = \Psi R(\lambda, A_0)(\lambda f) \ge 0$ for $\lambda > \max\{0,\omega\}$ and completes the proof. □

3 A model of a two phase cell cycle in a single cell line

The cell cycle is the period from cell birth to its division into daughter cells. It contains four major phases: G_1 phase (cell growth before DNA replicates), S phase (DNA synthesis and replication), G_2 phase (post DNA replication growth period), and M (mitotic) phase (period of cell division). The Smith–Martin model [36] divides the cell cycle into two phases: A and B. The A phase corresponds to all or part of G_1 phase of the cell cycle and has a variable duration, while the B phase covers the rest of the cell cycle. The cell enters the phase A after birth and waits for some random time T_A until a critical event occurs that is necessary for cell division. Then the cell enters the phase B which lasts for a finite fixed time T_B. At the end of the B-phase the cell splits into two daughter cells. We assume that individual states of the cell are characterized by age $a \ge 0$ in each phase and by size $x > 0$, which can be volume, mass, DNA content or any quantity conserved trough division. We assume that individual cells of size x increase their size over time in the same way, with growth rate $g(x)$ so that $dx/dt = g(x)$, and all cells age over time with unitary velocity so that $da/dt = 1$. We assume that the probability that a cell is still being in the phase A at age a is equal to $H(a)$, so the rate of exit from the phase A at age a is $\rho(a)$ given by

$$\rho(a) = -\frac{H'(a)}{H(a)}, \quad H(a) = \int_a^\infty h(r)\,dr, \tag{12}$$

where h is a probability density function defined on $[0,\infty)$, describing the distribution of the time T_A, the duration of the phase A. We make the following assumptions:

(I) The function h in (12) is a probability density function so that $h\colon [0,\infty) \to [0,\infty)$ is Borel measurable and the function H in (12) satisfies: $H(0) = 1$, $H(\infty) = 0$.

(II) The growth rate function $g\colon (0,\infty) \to (0,\infty)$ is globally Lipschitz continuous and $g(x) > 0$ for $x > 0$.

The Smith and Martin hypothesis [36] states that h is exponentially distributed with parameter $p > 0$, so that $\rho(a) = p$ for all $a > 0$. However, this does not agree with experimental data, see e.g. [18,43] for recent results. The generation time of a cell, i.e. the time from birth to division, can be written as $T = T_A + T_B$. Thus the distribution of the generation time has a probability density of the form

$$h_T(t) = \begin{cases} 0, & t < T_B \\ h(t - T_B), & t \geq T_B. \end{cases}$$

Cell generation times can have lognormal or bimodal distribution (see [35]), exponentially modified Gaussian [17], or tempered stable distributions [30].

To describe the growth of cells we define

$$\mathfrak{Q}(x) := \int_{\bar{x}}^{x} \frac{1}{g(r)} dr, \quad x > 0, \tag{13}$$

where $\bar{x} > 0$ or $\bar{x} = 0$, if the integral is finite. The value $\mathfrak{Q}(x)$ has a simple biological interpretation. If $\bar{x}$ is the size of a cell, then $\mathfrak{Q}(x)$ is the time it takes the cell to reach the size x. It follows from assumption (II) that the function $\mathfrak{Q}$ is strictly increasing and continuous. We denote by $\mathfrak{Q}^{-1}$ the inverse of $\mathfrak{Q}$. Define

$$\pi_t x_0 = \mathfrak{Q}^{-1}(\mathfrak{Q}(x_0) + t) \tag{14}$$

for $t \geq 0$ and $x_0 > 0$. Then $\pi_t x_0$ satisfies the initial value problem

$$x'(t) = g(x(t)), \quad x(0) = x_0 > 0.$$

If $\mathfrak{Q}(0) = -\infty$ then $\mathfrak{Q}^{-1}$ is defined on $\mathbb{R}$. Hence, formula (14) extends to all $t \in \mathbb{R}$ and $x_0 > 0$. We also set $\pi_t 0 = 0$ for $t > 0$ in this case. If $\mathfrak{Q}(0) = 0$ then $\mathfrak{Q}^{-1}$ is defined only on $(0,\infty)$ and we set $\pi_t 0 = \mathfrak{Q}^{-1}(t)$ for $t > 0$. We can extend formula (14) to all negative t satisfying $\mathfrak{Q}(x_0) + t > 0$; otherwise we set $\pi_t x_0 = 0$. Note that at time $t = T$, the generation time, a "mother cell" of size $\pi_T x_0$ divides into two daughter cells of equal size $\frac{1}{2}\pi_T x_0$.

In the probabilistic model of [22,25,38,39] a sequence of consecutive descendants of a single cell was studied. Let f be the probability density function of the size distribution at birth at time t_0 of mother cells and let $t_1 > t_0$ be a random time of birth of daughter cells. Then the probability density function of the size distribution of daughter cells is given by [25,38]

$$Pf(x) = -\int_0^{\lambda(x)} \frac{\partial}{\partial x} H(\mathfrak{Q}(\lambda(x)) - \mathfrak{Q}(r)) f(r)\, dr, \tag{15}$$

where

$$\lambda(x) = \max\{\pi_{-T_B}(2x), 0\} = \max\{\mathfrak{Q}^{-1}(\mathfrak{Q}(2x) - T_B), 0\}.$$

The iterates $P^2 f, P^3 f, \dots$ denote densities of the size distribution of consecutive descendants born at random times $t_2, t_3, \dots$. The operator P defined by (15) is a positive contraction on $L^1(0, \infty)$, the space of Borel measurable functions defined on $(0, \infty)$ and integrable with respect to the Lebesgue measure. Here we extend the probabilistic model to a continuous time situation by examining what happens at all times t and not only at $t_0, t_1, t_2, \dots$.

We denote by $p_1(t, a, x)$ and $p_2(t, a, x)$ the densities of the age and size distribution of cell in the A-phase and in the B-phase at time t, age a, and size x, respectively. Neglecting cell deaths the equations can be written as

$$\begin{aligned} \frac{\partial p_1(t,a,x)}{\partial t} + \frac{\partial p_1(t,a,x)}{\partial a} + \frac{\partial (g(x) p_1(t,a,x))}{\partial x} &= -\rho(a) p_1(t,a,x), \\ \frac{\partial p_2(t,a,x)}{\partial t} + \frac{\partial p_2(t,a,x)}{\partial a} + \frac{\partial (g(x) p_2(t,a,x))}{\partial x} &= 0, \end{aligned} \tag{16}$$

with boundary and initial conditions

$$p_1(t, 0, x) = 2p_2(t, T_B, 2x), \quad x > 0, t > 0, \tag{17}$$

$$p_2(t, 0, x) = \int_0^\infty \rho(a) p_1(t, a, x) da, \quad x > 0, t > 0, \tag{18}$$

$$p_1(0, a, x) = f_1(a, x), \quad p_2(0, a, x) = f_2(a, x). \tag{19}$$

In this model, cells in the A-phase enter the B-phase at rate ρ. This is taken into account by the boundary condition (18). All cells stay in the B-phase until they reach the age T_B. Then they divide their size into half (17). The model is complemented with initial conditions (19). The model we propose is different as compared to mass/maturity structured models [16,21,31,40] where a cell leaves the phase A with intensity being dependent on maturity, not age. In the case of $T_B = 0$ there is only one phase present; a maturity structured model being a continuous time extension of [24] is studied in [27], while age and volume/maturity structured population models of growth and division were studied extensively since the seminal work of [12,26,33]. We refer the reader to [28] for historical remarks concerning modeling of age structured populations and to [35,42] for recent reviews.

We look for positive solutions of (16)–(19) in the space $L^1 = L^1(E, \mathcal{E}, m)$ with $E = E_1 \times \{1\} \cup E_2 \times \{2\}$, where

$$E_1 = \{(a, x) \in (0, \infty) \times (0, \infty) : x > \pi_a 0\}$$

and

$$E_2 = \{(a, x) \in (0, T_B) \times (0, \infty) : x > \pi_a 0\},$$

m is the product of the two-dimensional Lebesgue measure and the counting measure on $\{1, 2\}$, and $\mathcal{E}$ is the σ-algebra of all Borel subsets of E. We identify $L^1 = L^1(E, \mathcal{E}, m)$ with the product of the spaces $L^1(E_1)$ and $L^1(E_2)$ of functions defined on the sets E_1 and E_2, respectively, and being integrable with respect to the two-dimensional Lebesgue measure. We say that the operator P has a steady state in $L^1(0,\infty)$ if there exists a probability density function f such that $Pf = f$. Similarly, a semigroup $\{S(t)\}_{t\geq 0}$ has a steady state in L^1 if there exists a nonnegative $f \in L^1$ such that $S(t)f = f$ for all $t > 0$ and $\|f\|_1 = 1$ where $\|\cdot\|_1$ is the norm in L^1.

Theorem 4 *Assume conditions* (I) *and* (II). *There exists a unique positive semigroup* $\{S(t)\}_{t\geq 0}$ *on* L^1 *which provides solutions of* (16)–(19) *and* $\{S(t)\}_{t\geq 0}$ *is stochastic. If* $H \in L^1(0,\infty)$ *then the semigroup* $\{S(t)\}_{t\geq 0}$ *has a steady state in* L^1 *if and only if the operator* P *in* (15) *has a steady state in* $L^1(0,\infty)$.

We give the proof of Theorem 4 in the next section. Theorem 4 combined with [9] implies the following sufficient conditions for the existence of steady states of (16)–(19).

Corollary 1 *Assume conditions* (I) *and* (II). *Suppose that* $H \in L^1(0,\infty)$ *and that* $|\mathfrak{Q}(0)| < \infty$. *If*

$$\mathbb{E}(T_A) := \int_0^\infty H(a)da < \liminf_{x\to\infty}(\mathfrak{Q}(\lambda(x)) - \mathfrak{Q}(x)) \tag{20}$$

then (16)–(19) *has a steady state and it is unique if, additionally,* $h(a) > 0$ *for all sufficiently large* a. *Conversely, if there is* $x_0 \geq 0$ *such that* $H(Q(\lambda(x_0))) > 0$ *and* $\mathbb{E}(T_A) > \sup_{x\geq x_0}(\mathfrak{Q}(\lambda(x)) - \mathfrak{Q}(x))$, *then* (16)–(19) *has no steady states.*

If the cell growth is exponential so that we have $g(x) = kx$ for all $x > 0$, where k is a positive constant, then it is known [22,38,39] that the operator P has no steady state. We now consider a linear cell growth and assume that $g(x) = k$ for all $x > 0$. We see that $\mathfrak{Q}(x) = x/k$, the operator P is of the form (see [39] or the last section)

$$Pf(x) = \frac{2}{k}\int_0^{2x-kT_B} h((2x - kT_B - r)/k)f(r)dr\mathbf{1}_{(0,\infty)}(2x - kT_B), \quad x > 0,$$

and condition (20) holds if and only if $\mathbb{E}(T_A) < \infty$. Combining Corollary 1 with Theorem 4 implies the following.

Corollary 2 *Assume that* $g(x) = k$ *for* $x > 0$ *and that* $h(a) > 0$ *for all sufficiently large* $a > 0$. *If* $\mathbb{E}(T_A) < \infty$ *then the semigroup* $\{S(t)\}_{t\geq 0}$ *has a unique steady state.*

4 Proof of Theorem 4

We will show that Theorem 4 can be deduced from Theorems 1 and 3. To this end, we introduce some notation. Let us define

$$\pi(t, a_0, x_0) = (a_0 + t, \pi_t x_0), \quad a_0, x_0 \geq 0, t \in \mathbb{R},$$

where π_t is given by (14). Then $t \mapsto \pi(t, a_0, x_0)$ solves the system of equations $a'(t) = 1$ and $x'(t) = g(x(t))$ with initial condition $a(0) = a_0$ and $x(0) = x_0$. Recall that E_1 is an open set. For any $x_0, a_0 \in E_1$ we define

$$t_-(a_0, x_0) = \inf\{s > 0 : \pi(-s, a_0, x_0) \notin \overline{E}_1\}$$

and the incoming part of the boundary ∂E_1

$$\Gamma_1^- = \{z \in \partial E_1 : z = \pi(-t_-(y), y) \text{ for some } y \in E_1 \text{ with } t_-(y) < \infty\}.$$

Observe that $t_-(a_0, x_0) = a_0$ for all $(a_0, x_0) \in E_1$ and that $\Gamma_1^- = \{0\} \times (0, \infty)$. We consider on Γ_1^- the Borel measure m_1^- being the product of the point measure δ_0 at 0 and the Lebesgue measure on $(0, \infty)$. We define the operator $\mathrm{T}_{\max}$ on $L^1(E_1)$ by [6]

$$\mathrm{T}_{\max} f(a, x) = -\frac{\partial(f(a, x))}{\partial a} - \frac{\partial(g(x)f(a, x))}{\partial x}$$

with domain

$$\mathcal{D}(\mathrm{T}_{\max}) = \{f \in L^1(E_1) : \mathrm{T}_{\max} f \in L^1(E_1)\},$$

where the differentiation is understood in the sense of distributions. Then it follows from [6] that for $f \in \mathcal{D}(\mathrm{T}_{\max})$ the following limit

$$\mathrm{B}^- f(z) = \lim_{t \to 0} f(\pi(t, z))$$

exists for almost every $z \in \Gamma_1^-$ with respect to the measure m_1^- on Γ_1^-. According to [6, Theorem 4.4] the operator $T_0 = \mathrm{T}_{\max}$ with domain

$$\mathcal{D}(\mathrm{T}_0) = \{f \in \mathcal{D}(\mathrm{T}_{\max}) : \mathrm{B}^- f = 0\}$$

is the generator of a substochastic semigroup on $L^1(E_1)$ given by

$$U_0(t)f(a, x) = \frac{g(\pi_{-t}x)}{g(x)} f(a - t, \pi_{-t}x)\mathbf{1}_{\{t < t_-(a,x)\}}(a, x), \quad (a, x) \in E_1,\ f \in L^1(E_1).$$

By [6, Proposition 5.1], the operator $(\mathrm{T}, \mathcal{D}(\mathrm{T}))$ defined by

$$\mathrm{T} f = \mathrm{T}_{\max} f - \rho f, \quad f \in \mathcal{D}(\mathrm{T}) = \{f \in \mathcal{D}(\mathrm{T}_0) : \rho f \in L^1(E_1)\}$$

is the generator of a substochastic semigroup on $L^1(E_1)$ of the from

$$U_1(t)f(a, x) = e^{-\int_0^t \rho(a-r)dr} U_0(t)f(a, x), \quad (a, x) \in E_1,\ f \in L^1(E_1).$$

Note that we can identify the space $L^1(E_2)$ with the subspace

$$Y = \{f \in L^1(E_1) : f(a,x) = 0 \text{ for a.e. } (a,x) \in E_1 \backslash E_2\}$$

of $L^1(E_1)$ and we have $\mathrm{T}_{\max}(\mathcal{D}(\mathrm{T}_{\max}) \cap L^1(E_2)) \subseteq L^1(E_2)$. We set

$$t_-(a_0,x_0) = \inf\{s > 0 : \pi(-s, a_0, x_0) \notin \overline{E_2}\} = a_0, \quad (a_0,x_0) \in E_2,$$

and

$$\Gamma_2^- = \{z \in \partial E_2 : z = \pi(-t_-(y), y) \text{ for some } y \in E_2 \text{ with } t_-(y) < \infty\}.$$

We also define the exit time from the set E_2 by

$$t_+(a_0,x_0) = \inf\{s > 0 : \pi(s, a_0, x_0) \notin \overline{E}_2\}$$

and the outgoing part of the boundary ∂E_2

$$\Gamma_2^+ = \{z \in \partial E_2 : z = \pi(t_+(y), y) \text{ for some } y \in E_2\}.$$

We have $t_+(a_0,x_0) = T_B - a_0$ and $\Gamma_2^+ = \{(T_B, x) : x > \pi_{T_B} 0\}$. We define the Borel measure m_2^- on Γ_2^- as the measure m_1^- and the m_2^+ on Γ_2^+ as the product of the point measure at T_B and the one dimensional Lebesgue measure. Since $U_0(t)(L^1(E_2)) \subseteq L^1(E_2)$, the part of the operator $(\mathrm{T}_0, \mathcal{D}(\mathrm{T}_0))$ in $L^1(E_2)$ is the generator of a substochastic semigroup $\{U_2(t)\}_{t\geq 0}$ in $L^1(E_2)$. Moreover, the following pointwise limits exist

$$\mathrm{B}^{\pm} f(z) = \lim_{t\to 0} f(\pi(\mp t, z)) \quad \text{for } f \in \mathcal{D}(\mathrm{T}_{\max}) \cap L^1(E_2)$$

for almost every $z \in \Gamma_2^{\pm}$ with respect to the Borel measure $m_2^{\pm}$ on $\Gamma_2^{\pm}$.

Let $E_\partial = \Gamma_1^- \times \{1\} \cup \Gamma_2^- \times \{2\}$, $\mathcal{E}_\partial$ be the σ-algebra of Borel subsets of E_∂ and m_∂ be the product of the Lebesgue measure on the line $\{0\} \times (0,\infty)$ and the counting measure on $\{1,2\}$. To simplify the notation we identify $L^1_\partial = L^1(E_\partial, \mathcal{E}_\partial, m_\partial)$ with the product space $L^1(0,\infty) \times L^1(0,\infty)$. We define operators A_1 and A_2 by

$$A_1 f_1 = \mathrm{T}_{\max} f_1 - \rho f_1, \quad f_1 \in \mathcal{D}_1 = \{f_1 \in L^1(E_1) : \mathrm{T}_{\max} f_1, \rho f_1 \in L^1(E_1)\}, \tag{21}$$

$$A_2 f_2 = \mathrm{T}_{\max} f_2, \quad f_2 \in \mathcal{D}_2 = \{f_2 \in L^1(E_2) : \mathrm{T}_{\max} f_2 \in L^1(E_2)\}. \tag{22}$$

We set

$$\mathcal{D} = \{(f_1, f_2) \in \mathcal{D}_1 \times \mathcal{D}_2 : \mathrm{B}^- f_1, \mathrm{B}^- f_2 \in L^1(0,\infty)\}$$

and we define the operator A on $\mathcal{D}$ by setting $Af = (A_1 f_1, A_2 f_2)$ for $f = (f_1, f_2) \in \mathcal{D}$. We take operators $\Psi_0, \Psi : \mathcal{D} \to L^1_\partial$ of the form

$$\Psi_0 f = (\mathrm{B}^- f_1, \mathrm{B}^- f_2), \quad f = (f_1, f_2) \in \mathcal{D}, \tag{23}$$

and

$$\Psi f(x) = \left(2\mathrm{B}^+ f_2(T_B, 2x)\mathbf{1}_{(\pi_{T_B}(0),\infty)}(2x), \int_0^\infty \rho(a) f_1(a, x)\mathbf{1}_{(0,\infty)}(\pi_{-a}x)da\right) \tag{24}$$

for $f = (f_1, f_2) \in \mathcal{D}$. We show that the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup on L^1, where $A_\Psi f = Af$ for $f \in \mathcal{D}(A_\Psi) = \{f \in \mathcal{D} : \Psi_0 f = \Psi f\}$. To this end, we check that assumptions (i)–(iv) of Theorem 1 from Sect. 2 are satisfied.

We first show that conditions (iii) and (iv) hold. The operator A restricted to $\mathcal{D}(A_0) = \{(f_1, f_2) \in \mathcal{D}_1 \times \mathcal{D}_2 : \mathrm{B}^- f_1 = 0, \mathrm{B}^- f_2 = 0\}$ is the generator of the semigroup $\{S_0(t)\}_{t\geq 0}$ given by

$$S_0(t)f = (U_1(t)f_1, U_2(t)f_2), \quad t \geq 0, f = (f_1, f_2) \in L^1,$$

since $\{U_1(t)\}_{t\geq 0}$ and $\{U_2(t)\}_{t\geq 0}$ are semigroups on the spaces $L^1(E_1)$ and $L^1(E_2)$ with the corresponding generators. The semigroup $\{S_0(t)\}_{t\geq 0}$ is substochastic. For all nonnegative $f = (f_1, f_2) \in \mathcal{D}$ we have

$$\begin{aligned}\int_E Af\,dm - \int_{E_\partial} \Psi_0 f\,dm_\partial = \int_{E_1} A_1 f_1(a, x)da dx + \int_{E_2} A_2 f_2(a, x)da dx \\ - \int_{\Gamma_1^-} \mathrm{B}^- f_1(z)m_1^-(dz) - \int_{\Gamma_2^-} \mathrm{B}^- f_2(z)m_2^-(dz).\end{aligned}$$

By [6, Proposition 4.6], this reduces to

$$\int_E Af\,dm - \int_{E_\partial} \Psi_0 f\,dm_\partial = -\int_{E_1} \rho(a) f_1(a, x)\,da dx - \int_{\Gamma_2^+} \mathrm{B}^+ f_2(z)m_2^+(dz), \tag{25}$$

implying that condition (iv) holds.

For $f = (f_1, f_2) \in \mathcal{D}$ we can rewrite the equation $\lambda f - Af = 0$ as

$$\begin{aligned}\frac{\partial}{\partial a}\left(e^{\int_0^a \rho(r)dr} f_1(a, x)\right) &= -\frac{\partial}{\partial x}(g(x) f_1(a, x)) - \lambda f_1(a, x), \\ \frac{\partial}{\partial a}(f_2(a, x)) &= -\frac{\partial}{\partial x}(g(x) f_2(a, x)) - \lambda f_2(a, x).\end{aligned}$$

Hence, we see that the right inverse of Ψ_0 when restricted to the nullspace of $\lambda I - A$ is given by

$$\Psi(\lambda)f_\partial(a,x) = \left(e^{-\lambda a - \int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x), e^{-\lambda a} f_{\partial,2}(\pi_{-a}x)\mathbf{1}_{(0,T_B)}(a)\right) \frac{g(\pi_{-a}x)}{g(x)} \tag{26}$$

for $(a,x) \in E_1$ and $f_\partial = (f_{\partial,1}, f_{\partial,2}) \in L^1_\partial$. Moreover, if $(f_1, f_2) = \Psi(\lambda)f_\partial$ then

$$\mathrm{B}^- f_1(0,x) = \lim_{t\to 0} f_1(t, \pi_t x) = \lim_{t\to 0} e^{-\lambda t - \int_0^t \rho(r)dr} f_{\partial,1}(x) = f_{\partial,1}(x).$$

Thus $f_1 \in \mathcal{D}_1$. Similarly, $f_2 \in \mathcal{D}_2$. Hence, condition (i) holds.

To check condition (ii) take $\lambda > 0$ and $f_\partial \in L^1_\partial$. For $(f_1, f_2) = \Psi(\lambda)f_\partial$ we have

$$f_2(a,x) = e^{-\lambda a} f_{\partial,2}(\pi_{-a}x)\frac{g(\pi_{-a}x)}{g(x)}\mathbf{1}_{(0,\infty)}(\pi_{-a}x)\mathbf{1}_{(0,T_B)}(a).$$

This implies that

$$\begin{aligned}
\mathrm{B}^+ f_2(T_B, x) &= \lim_{t\to 0} f_2(T_B - t, \pi_{-t}x)\\
&= \lim_{t\to 0} e^{-\lambda(T_B - t)} f_{\partial,2}(\pi_{-T_B}x)\frac{g(\pi_{-T_B}x)}{g(\pi_{-t}x)}\mathbf{1}_{(0,\infty)}(\pi_{-T_B}x)\\
&= e^{-\lambda T_B} f_{\partial,2}(\pi_{-T_B}x)\frac{g(\pi_{-T_B}x)}{g(x)}\mathbf{1}_{(0,\infty)}(\pi_{-T_B}x).
\end{aligned}$$

Hence,

$$\Psi\Psi(\lambda)f_\partial(x) = ((\Psi\Psi(\lambda)f_\partial)_1(x), (\Psi\Psi(\lambda)f_\partial)_2(x)),$$

where

$$(\Psi\Psi(\lambda)f_\partial)_1(x) = 2e^{-\lambda T_B} f_{\partial,2}(\pi_{-T_B}(2x))\frac{g(\pi_{-T_B}(2x))}{g(2x)}\mathbf{1}_{(0,\infty)}(\pi_{-T_B}(2x))$$

and, by (12),

$$(\Psi\Psi(\lambda)f_\partial)_2(x) = \int_0^\infty h(a)e^{-\lambda a} f_{\partial,1}(\pi_{-a}x)\frac{g(\pi_{-a}x)}{g(x)}\mathbf{1}_{(0,\infty)}(\pi_{-a}x)da.$$

For $f_\partial \in L^1_\partial$ we obtain

$$\begin{aligned}
\|\Psi\Psi(\lambda)f_\partial\| &\le e^{-\lambda T_B}\int_0^\infty |f_{\partial,2}(z)|dz + \int_0^\infty h(a)e^{-\lambda a}da \int_0^\infty |f_{\partial,1}(y)|dy\\
&\le \max\left\{e^{-\lambda T_B}, \int_0^\infty h(a)e^{-\lambda a}da\right\}\|f_\partial\|,
\end{aligned}$$

showing that $\|\Psi\Psi(\lambda)\| < 1$ for all $\lambda > 0$. Consequently, it follows from Theorem 1 that the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup $\{S(t)\}_{t\geq 0}$ on L^1. The semigroup $\{S(t)\}_{t\geq 0}$ is stochastic, since (8) holds by (25).

Next assume that $H \in L^1(0,\infty)$. By Theorem 3, it remains to look for fixed points of the operator $\Psi\Psi(0)$. Here $\Psi(0)$ defined as in (11) is, by (26), of the form

$$\Psi(0)f_\partial(a,x) = \left(e^{-\int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x),\, f_{\partial,2}(\pi_{-a}x)\mathbf{1}_{[0,T_B)}(a)\right)\frac{g(\pi_{-a}x)}{g(x)} \tag{27}$$

for $(a,x) \in E_1$. Observe that $\Psi(0)f_\partial \in L^1$ for $f_\partial \in L^1_\partial$, since $e^{-\int_0^a \rho(r)dr} = H(a)$, by (12), and

$$\|\Psi(0)f_\partial\| \le \int_0^\infty H(a)da \int_0^\infty |f_{\partial,1}(y)|dy + T_B \int_0^\infty |f_{\partial,2}(y)|dy.$$

We have $\pi_{-T_B}(2x) = \mho^{-1}(\mho(2x) - T_B) = \lambda(x)$ if $2x > \pi_{T_B}0$ and

$$\lambda'(x) = 2\frac{g(\lambda(x))}{g(2x)}\mathbf{1}_{(0,\infty)}(\lambda(x)). \tag{28}$$

Hence

$$(\Psi\Psi(0)f_\partial)_1(x) = f_{\partial,2}(\lambda(x))\lambda'(x)$$

and

$$(\Psi\Psi(0)f_\partial)_2(x) = \int_0^\infty \rho(a)e^{-\int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x)\frac{g(\pi_{-a}x)}{g(x)}\mathbf{1}_{(0,\infty)}(\pi_{-a}x)da.$$

If $f_\partial = \Psi\Psi(0)f_\partial$ then $f_{\partial,2}(x) = (\Psi\Psi(0)f_\partial)_2(x)$ and $f_{\partial,1}$ satisfies

$$\begin{aligned} f_{\partial,1}(x) &= (\Psi\Psi(0)f_\partial)_1(x) \\ &= 2\int_0^\infty h(a)f_{\partial,1}(\pi_{-a}(\lambda(x)))\frac{g(\pi_{-a}(\lambda(x)))}{g(2x)}\mathbf{1}_{(0,\infty)}(\pi_{-a}(\lambda(x)))da. \end{aligned}$$

By changing the variables $r = \pi_{-a}(\lambda(x))$, we arrive at the equation

$$f_{\partial,1}(x) = \frac{2}{g(2x)}\int_0^{\lambda(x)} h(\mho(\lambda(x)) - \mho(r))f_{\partial,1}(r)dr, \quad x > 0. \tag{29}$$

Equivalently, $f_{\partial,1} = Pf_{\partial,1}$ where P is as in (15). Consequently, equation $\Psi\Psi(0)f_\partial = f_\partial$ has a solution in L^1_∂ if and only if the equation $Pf_{\partial,1} = f_{\partial,1}$ has a solution in $L^1(0,\infty)$. Observe also that the operator $\Psi\Psi(0)$ preserves the L^1_∂ norm on nonnegative elements. Hence, if $f_\partial \in L^1_\partial$ is such that $\Psi\Psi(0)f_\partial \le f_\partial$ then $\Psi\Psi(0)f_\partial = f_\partial$. Thus the assertion follows from Theorem 3.

5 Final remarks

Our model can be described as a piecewise deterministic Markov process $\{X(t)\}_{t\geq 0}$. We considered three variables (a, x, i), where $i = 1$ if a cell is in the phase A, $i = 2$ if it is in the phase B, the variable x describes the cell size, and a describes the time which elapsed since the cell entered the ith phase. Let $t_0 = 0$. If we observe consecutive descendants of a given cell and the nth generation time is denoted by t_n, then $t_{n+1} = s_n + T_B$ where s_n is the time when the cell from the nth generation enters the phase B, $n \geq 0$. A newborn cell at time t_n is with age $a(t_n) = 0$ and with initial size equal to $x(t_n^-)/2$, where $x(t_n^-)$ is the size of its mother cell. The cell ages with velocity 1 and its size grows according to the equations $x'(t) = g(x(t))$ for $t \in (t_n, s_n)$. If the cell enters the phase B then its age is reset to 0 and its size still grows according to $x'(t) = g(x(t))$ for $t \in (s_n, s_n + T_B)$. We have

$$a(s_n) = 0, \quad x(s_n) = x(s_n^-), \quad i(s_n) = 2, \tag{30}$$

and at the end of the second phase the cell divides into two cells, so that we have

$$a(t_{n+1}) = 0, \quad x(t_{n+1}) = \frac{1}{2}x(t_{n+1}^-), \quad i(t_{n+1}) = 1. \tag{31}$$

Thus the process $X(t) = (a(t), x(t), i(t))$ satisfies the following system of ordinary differential equations

$$a'(t) = 1, \quad x'(t) = g(x(t)), \quad i'(t) = 0,$$

between consecutive times $t_0, s_0, t_1, s_1, \ldots$, called *jump times*. At jump times the process is given by (30) and (31). If the distribution of $X(0)$ has a density f then $X(t)$ has a density $S(t)f$, i.e.,

$$\Pr(X(t) \in B_i \times \{i\}) = \int_{B_i} (S(t)f)_i(a, x)dadx$$

for any Borel set $B_i \subset E_i$, where $\{S(t)\}_{t\geq 0}$ is the stochastic semigroup from Theorem 4.

If $f_{\partial,1}$ is the density of the size distribution at time $t_0 = 0$ and $f_{\partial,2}$ is the density of the distribution of size at time s_1, then the distribution of size at time t_1 is given by

$$\Pr(x(t_1) \leq x) = \Pr(\pi_{T_B} x(s_1) \leq 2x) = \Pr(x(s_1) \leq \lambda(x)) = \int_0^{\lambda(x)} f_{\partial,2}(z)dz$$

and

$$f_{\partial,2}(z) = \int_0^{\infty} h(a)\hat{\pi}_a f_{\partial,1}(z)da, \tag{32}$$

where

$$\hat{\pi}_a f_{\partial,1}(z) = f_{\partial,1}(\pi_{-a}z)\frac{g(\pi_{-a}z)}{g(z)}\mathbf{1}_{(0,\infty)}(\pi_{-a}z)$$

is the density of the size $x(a)$ of the cell at time a, if $x(0)$ has a density $f_{\partial,1}$. Thus the density of the mass $x(t_1)$ is given by

$$\frac{d}{dx}\Pr(x(t_1) \le x) = f_{\partial,2}(\lambda(x))\lambda'(x) = Pf_{\partial,1}(x)$$

for Lebesgue almost every $x \in (0,\infty)$, where P is as in (15). Now, if the operator P has a steady state $f_{\partial,1} \in L^1(0,\infty)$ so that $f_{\partial,1}$ satisfies (29) and if $f_{\partial,2}$ is as in (32), then $f^* = (f_1^*, f_2^*)$ given by

$$f_1^*(a,x) = e^{-\int_0^a \rho(r)dr}\hat{\pi}_a f_{\partial,1}(x), \quad f_2^*(a,x) = \hat{\pi}_a f_{\partial,2}(x)\mathbf{1}_{(0,T_B)}(a) \tag{33}$$

is the steady state for the semigroup $\{S(t)\}_{t\ge 0}$ existing by Theorem 4. Moreover, it is unique if P has a unique steady state.

Remark 6 It should be noted that in the two-phase cell cycle model in [31] the rate of exit from the phase A depends on x, not on a, and that there is no such equivalence between the existence of steady states as presented in Theorem 4. Our results remain true if we assume as in [31] that division into unequal parts takes place. Methods as in [31,34] can also be used in our model to study asymptotic behaviour of the semigroup $\{S(t)\}_{t\ge 0}$. For a different approach to study positivity and asymptotic behaviour of solutions of population equations in L^1 we refer to [32].

We conclude this section with an extension of the age-size dependent model from [12] to a model with two phases. Let $p_i(t,a,x)$ be the function representing the distribution of cells over all individual states a and x at time t in the phase A for $i=1$ or B for $i=2$, i.e., $\int_{a_1}^{a_2}\int_{x_1}^{x_2} p_i(t,a,x)dadx$ is the number of cells with age between a_1 and a_2 and size between x_1 and x_2 at time t in the given phase. Then p_1 and p_2 satisfy Eqs. (16), (18), (19) while the boundary condition (17) takes the form

$$p_1(t,0,x) = 4p_2(t,T_B,2x), \quad x>0,\ t>0, \tag{34}$$

since a mother cell at the moment of division T_B has size $2x$ and gives birth to two daughters of size x entering the phase A at age 0.

Theorem 5 *Assume conditions* (I) *and* (II). *Then there exists a unique positive semigroup on L^1 which provides solutions of* (16), (34), (18), (19).

This follows from Theorem 1 in the same way as Theorem 4, where now to check condition (ii) we note that

$$\|\Psi\Psi(\lambda)f_\partial\| \le \max\left\{2e^{-\lambda T_B}, \int_0^\infty h(a)e^{-\lambda a}da\right\}\|f_\partial\|$$

for all $f_\partial \in L^1_\partial$ and $\lambda > 0$, implying that $\|\Psi\Psi(\lambda)\| < 1$ for all $\lambda > \omega$ with $\omega = \log 2/T_B$.

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